

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-51. (Canceled)

52. **(Withdrawn, previously amended)** A method for the long term culture of hepatocyte cells or at least one non-hepatocyte cell type, wherein the said at least one non-hepatocyte cell type is selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells, said method comprising the steps of:

comminuting hepatocyte tissue in cold DMEM and incubating for up to 24 hours at 4°C;

twice digesting with liberase[®] at a concentration of 0.2mg/ml in the presence of lignocaine;

separating the digested hepatocyte cells; and

culturing in medium comprising allogeneic serum,

wherein said hepatocyte cells or non-hepatocyte cells are capable of secreting one or more liver secretory factors for extended periods in culture.

53. **(Withdrawn)** The method of claim 52, wherein the hepatocytes are neonatal hepatocytes.

54. **(Withdrawn)** The method of claim 52, further including the step of co-culturing the non-hepatocyte cells with the hepatocyte cells.

55. **(Withdrawn)** The method of claim 54, wherein the non-hepatocyte cells and/or hepatocyte cells are neonatal cells.

56. **(Withdrawn)** The method of 53, wherein the at least one non-hepatocyte cell type and/or hepatocytes are pig or human cells.

57. **(Withdrawn)** The method of claim 52, wherein the one or more liver secretory factors are selected from the group comprising albumin, blood clotting factors such as factor VIII or factor IX, growth and/or differentiation factors such as growth hormone and analogues thereof, insulin-like growth factor and analogues thereof, hepatocyte growth factor and analogue thereof, fibroblast growth factor and analogues thereof; or hormones such as corticosteroids.

58. **(Withdrawn)** A method of producing one or more liver secretory factors in vitro from at least one non-hepatocyte cell type selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells, said method comprising the steps of:

- isolating said at least one non-hepatocyte cell type;
- culturing said at least one non-hepatocyte cell type in a medium supplemented with allogeneic serum for a time sufficient to allow secretion of said one or more liver secretory factors into the media;
- harvesting said medium; and
- optionally isolating or purifying said liver secretory factors.

59. **(Withdrawn)** The method of claim 58, wherein the at least one non-hepatocyte cell type is co-cultured with hepatocyte cells.

60. **(Withdrawn)** The method of claim 58, wherein said at least one non-hepatocyte cell type is isolated from neonatal tissue.

61. **(Withdrawn)** The method of claim 58, wherein said at least one non-hepatocyte cell is a pig or human cell.

62. **(Currently amended)** An implantable composition comprising hepatocyte cells and at least one non-hepatocyte ~~cell type~~ cell, said non hepatocytes being capable upon implantation into a recipient of secreting one or more liver secretory factors or of providing one or more liver metabolic and/or physiologic functions to said recipient, wherein said composition comprises cells or aggregates thereof, wherein said one or more neonatal non-hepatocyte cell type is selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells, wherein said non-hepatocyte cell type maintains its ~~cell~~ secretory phenotype, and wherein the ratio of hepatocyte cell number to non-hepatocyte cell number is between 0.5:2 and 2:0.5.

63-65. **(Canceled)**

66. **(Currently amended)** The composition of claim 62, wherein the at least one non-hepatocyte cell ~~type~~ is a pig or human cell.

67. **(Currently amended)** The composition of claim 62, wherein the at least one non-hepatocyte cell ~~type~~ comprises gall bladder endothelial and/or epithelial cells.

68. **(Previously presented)** The composition of claim 62, comprising gall bladder epithelial cells.

69. **(Currently amended)** The composition of claim 62 ~~further comprising hepatocytes, wherein there is a ratio of cells of between 0.5:2 and 2:0.5 gall bladder epithelial cells: hepatocytes~~ epithelial cell number to hepatocyte cell number of 1:1..

70. **(Previously presented)** The composition of claim 62, wherein the one or more liver secretory factors is a blood clotting factor.

71. **(Previously presented)** The composition of claim 62, wherein the one or more liver secretor factors is Factor VIII and/or Factor IX.

72. **(Previously presented)** The composition of claim 62, wherein the one or more liver secretory factors is Factor VIII, and von Willebrand factor.

73. **(Previously presented)** The composition of claim 62, wherein the one or more liver secretory factors is a growth and/or differentiation factor.

74. **(Previously presented)** The composition of claim 62, wherein the one or more liver secretory factors is an enzyme.

75. **(Previously presented)** The composition of claim 62, wherein said non-hepatocyte cell types are derived from the same species as the recipient.

76. **(Withdrawn)** A method of producing one or more liver secretory factors in vivo, comprising the step of implanting an effective amount of a composition as claimed in claim 62 into a patient in need thereof.

77. **(Withdrawn)** The method of claim 76, wherein said composition provides liver secretory factors or provides liver metabolic or physiologic functions over an extended period post implantation.

78. **(Withdrawn)** A method of treating a patient suffering from or predisposed to a disease or condition associated with a deficiency in or absence of a liver secreted factor comprising the implantation of an effective amount of one or more implantable compositions of claim 62 to a patient in need thereof.

79. **(Withdrawn, previously amended)** The method of claim 78, wherein said disease or condition is selected from the group of diseases consisting of chronic liver insufficiency, liver failure, liver disease and alcoholic liver disease.

80. **(Withdrawn)** The method of claim 78, wherein said disease or condition is caused by infection with hepatitis A or B virus.

81. **(Withdrawn)** The method of claim 78, wherein the disease or condition is a blood clotting disease or condition.

82. **(Withdrawn)** The method of claim 81, wherein the blood clotting disease or condition is a hemophilia.

83. **(Withdrawn)** The method of claim 82, wherein said hemophilia is hemophilia A.

84. **(Withdrawn)** The method of claim 78, wherein the implantable composition comprises cells encapsulated in a suitable biocompatible material such as alginate; cells confined in a suitable device, such as a vascularized tube or TheracyteTM device; cells encapsulated in matrix preparations such as gelatin, collagen, and/or natural carbohydrate polymers; and/or cells confined in a plasma thrombin clot including allogeneic plasma clots produced with allogeneic thrombin.

85. **(Withdrawn)** A method of administering a blood clotting factor to a patient in need thereof, wherein said blood clotting factor is complexed and/or associated with one or more factors capable of enhancing the activity, stability, bioavailability, and/or efficacy of said blood clotting factor, wherein the method comprises the implantation of an effective amount of one or more implantable compositions of claim 62 to said patient.

86. **(Withdrawn)** The method of claim 85, wherein the blood clotting factor is Factor VIII, and said one or more factors capable of enhancing the activity, stability, bioavailability, and/or efficacy of said blood clotting factor is von Willebrand factor.

87. **(Withdrawn)** A method of treating a patient suffering from or predisposed to a disease or condition associated with a deficiency in a metabolic and/or physiologic function of the liver, said method comprising the implantation of an effective amount of one or more implantable compositions of claim 62 to the patient.

88. **(Withdrawn)** The method of claim 87, wherein the disease or condition comprises chronic liver insufficiency, liver failure, liver disease, or alcoholic liver disease.

89. **(Previously presented)** A device for implantation into a recipient suffering from or predisposed to a disease associated with a deficiency in or absence of a secreted liver factor, the device comprising one or more implantable compositions of claim 62.

90. **(Canceled)**

91. **(Currently amended)** The device of claim ~~90~~, 94, wherein the hepatocytes are isolated from immortalised cells in commercially available cell cultures.

92. **(Previously presented)** The device of claim ~~90~~, 94, wherein the biocompatible material is alginate.

93. **(Previously presented)** The device of claim ~~90~~, 94, wherein the plasma thrombin clot is an allogeneic plasma clot produced with allogeneic thrombin.

94. **(New)** A device for implantation into a recipient suffering from or predisposed

to a disease associated with a deficiency in or absence of a secreted liver factor, the device comprising

- (i) a capsule comprising a suitable biocompatible material;
- (ii) a vascularized tube or chamber;
- (iii) a subcutaneous implant device which is impermeable to cells but permeable to proteins and secreted factors;
- (iv) a matrix preparation comprising gelatin, collagen, or natural carbohydrate polymers or a plasma thrombin clot; and
- (v) one or more implantable compositions comprising hepatocytes and at least one neonatal non-hepatocyte cell, wherein said non-hepatocyte cell is capable, upon implantation into a recipient, of secreting one or more liver secretory factors or of providing one or more liver metabolic and/or physiologic functions to said recipient, wherein said composition comprises cells or aggregates thereof, wherein said one or more neonatal non-hepatocyte cell is selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells, wherein said non-hepatocyte cell maintains its secretory phenotype, and wherein there is a ratio of hepatocyte cell number to non-hepatocyte cell number between 0.5:2 and 2:0.5 in said one or more implantable compositions.